

iS

(FILE 'HOME' ENTERED AT 18:51:56 ON 08 MAR 2002)

FILE 'MEDLINE, CANCERLIT, EMBASE, BIOSIS, CAPLUS, BIOTECHDS' ENTERED AT
18:52:15 ON 08 MAR 2002

L1	47 S DODAP
L2	1441294 S IMMUNE OR ADJUVANT
L3	1 S L1 AND L2
L4	1 DUP REM L3 (0 DUPLICATES REMOVED)
L5	1267980 S IMMUNOGEN OR ANTIGEN
L6	0 S L5 AND L1
L7	295484 S VACCINE OR IMMUNOGENIC
L8	1 S L7 AND L1
L9	25 DUP REM L1 (22 DUPLICATES REMOVED)
L10	42 S CATIONIC LIPID AND ADJUVANT
L11	18 DUP REM L10 (24 DUPLICATES REMOVED)

=>

L11 ANSWER 16 OF 18 MEDLINE
 AN 1999294420 MEDLINE
 DN 99294420 PubMed ID: 10367954
 TI **Cationic lipid** DC-Chol induces an improved and
 balanced immunity able to overcome the unresponsiveness to the hepatitis B
 vaccine.
 AU Brunel F; Darbouret A; Ronco J
 CS Research Department, Pasteur Merieux Connaught, Marcy L'Etoile, France.
 SO VACCINE, (1999 Apr 23) 17 (17) 2192-203.
 Journal code: X60; 8406899. ISSN: 0264-410X.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199907
 ED Entered STN: 19990806
 Last Updated on STN: 19990806
 Entered Medline: 19990727
 AB Th1 and Th2 immune responses against antigens can be modulated by the use
 of adjuvants. Since antibody isotypes (IgG1 and IgG2a) and cytokines
 induced may reflect the Th differentiation taking place during the immune
 response, the humoral and cellular immune responses induced in mice
 against hepatitis B virus surface antigen (HBsAg) were examined when the
 antigen was either adsorbed to aluminum hydroxyde or administered with a
 new **adjuvant the cationic lipid**
 3beta-[N-(N',N'-dimethylaminoethane)carbamoyl]cholesterol (DC-Chol). The
 use of DC-Chol increased antibody responses in responding BALB/c mice,
 induced more consistent IgG1 and IgG2a antibody responses in OF1 mice and
 overcame the nonresponse to HBsAg in B10.M mice. Furthermore, DC-Chol was
 able to induce cellular immune responses to HBsAg. The DC-Chol induced a
 balanced Th1/Th2 response, which enabled mice to overcome the inherited
 unresponsiveness to HBsAg encountered with aluminum-adjuvanted vaccine.
 Thus, the DC-Chol provides a signal to switch on both Th1 and Th2
 responses, which may have important implications for vaccination against
 hepatitis B virus, as well as for enhancing weak immunogenicity of other
 recombinant purified antigens in a nonresponder population.

L11 ANSWER 12 OF 18 MEDLINE
AN 2000385150 MEDLINE
DN 20227408 PubMed ID: 10766341
TI Activation of host antitumoral responses by **cationic lipid**/DNA complexes.
AU Bramson J L; Bodner C A; Graham R W
CS Inex Pharmaceuticals Corporation, Burnaby, British Columbia, Canada..
bramsonj@FHS.mcmaster.ca
SO CANCER GENE THERAPY, (2000 Mar) 7 (3) 353-9.
Journal code: CE3; 9432230. ISSN: 0929-1903.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000804
AB A model of lipoplex-induced peritonitis was used to characterize the inflammatory response to **cationic lipid**:DNA lipoplexes with respect to activation of host antitumoral effector mechanisms. Three different cationic lipids were used in these studies: N,N-dioleoyl-N,N-dimethylammonium chloride (DODAC), N-(1-[2,3-dioleoyloxy]propyl)-N,N,N-trimethylammonium chloride (DOTAP), and N-(1-[2,3-dioleoyloxy]propyl)-N,N,N-trimethylammonium chloride (DOTMA). The DODAC and DOTMA lipoplexes exhibited similar transfection properties in vitro, whereas the DOTAP lipoplexes transfected quite poorly in all cell lines tested. Intraperitoneal injection of cationic lipoplexes into immunocompetent mice resulted in a profound infiltration of inflammatory cells, secretion of interferon-gamma, and increased natural killer activity within the peritoneal cavity. Both DODAC and DOTMA lipoplexes produced similar inflammatory responses, lasting at least 5 days. The inflammation induced by DOTAP lipoplexes peaked by day 3 and resolved to near-control levels by day 5. These data indicate that although **cationic lipid** DNA complexes may differ in their inflammatory properties, the natural killer activation and interferon-gamma secretion that follow lipoplex administration should provide a functional **adjuvant** for cancer gene therapies that benefit from immunostimulation.

L11 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2002 ACS
 AN 2000:861646 CAPLUS
 DN 134:21482
 TI Cytofectin dimers and methods of use thereof
 IN Wheeler, Carl J.
 PA Vical, Inc., USA
 SO PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000073263	A1	20001207	WO 2000-US14676	20000526
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1183231	A1	20020306	EP 2000-939373	20000526
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1999-136472	P	19990528		
	WO 2000-US14676	W	20000526		

OS MARPAT 134:21482

AB A compn. is provided comprising a novel **cationic lipid** compd. having hydrophobic tails and two quaternary ammonium headgroups bridged by a linker. The compn. is useful as a cytofectin for facilitating delivery and transfection of biol. active agents, particularly anionic bioactive agents such as DNA, into cells. The compn. is useful also as an **adjuvant** for enhancing the humoral immune response of a vertebrate to an immunogen, esp. an immunogen encoded by a polynucleotide-based vaccine. In certain preferred embodiments, the **cationic lipid** compd. is a dimer contg. quaternary ammonium headgroups bridged by a linker having DNA and/or cell receptor binding affinity, such as a polypeptide or polyamine. Also disclosed is an immunogenic compn. comprising an immunogen and the compn. of the present invention. I was prepd. as an example compd.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 18 MEDLINE DUPLICATE 3
AN 2001546235 MEDLINE

DN 21477224 PubMed ID: 11592838

TI Antitumor activity of **cationic lipid** complexed with immunostimulatory DNA.

AU Rudginsky S; Siders W; Ingram L; Marshall J; Scheule R; Kaplan J

CS Genzyme Corporation, Framingham, Massachusetts 01701, USA.

SO MOLECULAR THERAPY, (2001 Oct) 4 (4) 347-55.

Journal code: 100890581. ISSN: 1525-0016.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200112

ED Entered STN: 20011011

Last Updated on STN: 20020122

Entered Medline: 20011212

AB We previously reported that treatment of intraperitoneal tumors with complexes of **cationic lipid** and noncoding plasmid DNA leads to the development of a specific, cytotoxic T-cell response correlating with the rejection of established tumor cells as well as subsequent tumor re-challenge. Here, focusing on an intraperitoneal AB12 mesothelioma model, we show that the anticancer effects of the lipid:DNA complex are associated with DNA containing immunostimulatory CpG motifs. Complexes prepared with **cationic lipid** and bacterial plasmid DNA, Escherichia coli genomic DNA fragments, or synthetic immunostimulatory CpG oligodeoxynucleotides provided a substantial survival benefit, whereas eukaryotic DNA and methylated bacterial DNA had little or no therapeutic activity. Alternative inflammatory stimuli such as thioglycolate, poly(I:C), and incomplete or complete Freund's **adjuvant** failed to reproduce the antitumor activity obtained with the lipid:DNA complex. The innate immune response triggered by lipid:DNA complexes led to the development of a systemic immune response against tumor cells that allowed animals to reject tumors not only at the intraperitoneal treatment site, but also at a distal subcutaneous site. These data demonstrate that immunostimulatory DNA complexed with **cationic lipid** is a potent inducer of innate and adaptive immune responses against tumor cells and represents a potentially useful tool in the immunotherapy of cancers for which tumor-associated antigens have not been identified.